

psychological factors involved, such temporary improvement must be interpreted with caution.

3. Treatment with desoxycorticosterone acetate and ascorbic acid for periods up to fourteen days was found to have no effect on the activity or the progression of the diseases as shown by the degree of swelling, the erythrocyte sedimentation rate and serum protein fractions.

4. The injection of desoxycorticosterone acetate and ascorbic acid did not have any effect on the total circulating eosinophil counts or glucose tolerance curves such as are found after therapy with cortisone or ACTH.

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FLAXEDIL,* A NEW CURARIZING AGENT

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SINCE Griffiths¹ first used curare (an alkaloid prepared from several South American plants) for the purpose of obtaining muscular relaxation during general anaesthesia in 1942, research has been directed towards preparing synthetic muscular relaxants which would necessarily have a more constant amount of active principle and also a more reliable source of the raw materials, and possibly less of the undesirable effects of curare such as respiratory depression, hypotension and bronchospasm,² the latter two of which are due to the liberation of histamine.³

Bovet and Halpern *et al.*,^{4, 5} working in the research laboratories of Rhône-Poulenc-Specia in France investigated the pharmacological properties of several synthetic curarizing agents 3,381 R.P.; 3,602 R.P.; 3,565 R.P., etc. The compound 3,697 R.P., (flaxedil) was finally selected for clinical study and the first

clinical trial on 127 cases was reported on by Huguenard and Boué in 1948.⁶ Mushin *et al.*⁷ reported in April, 1949, on the effect of flaxedil on cats, conscious human volunteers, and on 45 adult patients undergoing major abdominal operations under cyclopropane or light ether anaesthesia.

The present paper is a report based on the administration of flaxedil to 100 patients undergoing surgery between April 16 and August 19, 1949. The results are compared in part with a similar series of 100 patients who received d-tubo-curarine chloride as the relaxing agent.

Chemical constitution.—Flaxedil is tri-(diethyl amino-ethoxy) benzene tri-ethyl iodide, (C₃₀ H₅₀ O₃ N₃ I₃). It has a molecular weight of 891. In pure form it occurs as a white, amorphous, odourless, slightly bitter tasting powder. It has a melting point between 145 and 150° C. It is very soluble in water, in ethyl alcohol and in methyl alcohol. It is slightly soluble in ether, benzene and chloroform.

Pharmacology: action on muscles.—Flaxedil in adequate dosage relaxes striated muscle, apparently in the same manner as curare,⁸ *i.e.*, by preventing the muscle response to nerve stimulation, probably by direct action on the receptor substance in the muscle. Complete relaxation of the flexor muscles of the forearm and the abdominal muscles, without decreasing respiratory volume, can be obtained in the conscious volunteer with dosages of about one mgm. per kg. of body weight.⁷ The order of relaxation is the same as with curare, *i.e.*, eyelids, jaws, extremities, abdominal muscles, the glottis and lastly the diaphragm. The margin of safety between abdominal relaxation and diaphragmatic paralysis is slightly greater than with d-tubo-curarine chloride.⁷ The paralyzing effect can be quickly reversed, as with curare, by the intravenous injection of prostigmine, 0.5 to 2.5 mgm. in 1/2,000 solution. This must always be preceded by atropine 1/150 to 1/200 gr. intravenously.

Circulatory system.—Vascular tone is not depressed and the myocardium is unaffected. Bleeding and clotting time are not prolonged. There is no fall in blood pressure in dogs even with many times the paralyzing dose.

Autonomic nervous system.—There is no effect on the bowel and vomiting is not induced in man or animals. The skin appearance is unaltered and there is no increase in salivary or bronchial secretions. There is a complete absence of any histamine effect which has been reported with curare.³ to ⁹

Toxicity.—Flaxedil is 1/5 as toxic as curare in mice and 500 times the curarizing dose in rabbits under artificial respiration is necessary to kill.

Clinical application.—The first few cases in which flaxedil was used in this series were of a minor nature and only small doses were used. As confidence was gained, no selection of cases was made until near the end of the series when patients with a very rapid pulse or who were thought likely to develop tachycardia were not given the drug or it was used in conjunction with d-tubo-curarine chloride. For purpose of comparison 100 similar cases who had received curare were selected from my case cards by a disinterested observer, the basis of selection

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being the type of operation and age. These latter cases had all been operated on during the past year.

Preoperative sedation.—In both series this consisted of medinal gr. 5 or seconal sodium gr. $1\frac{1}{2}$ the night before operation and morphine gr. $\frac{1}{6}$ or demerol 100 mgm. with atropine $\frac{1}{150}$ gr. one hour preoperatively. These doses were altered slightly on occasion to suit the case.

Method of administration.—All cases were induced with pentothal $2\frac{1}{2}\%$ and all cases were carried on approximately 60% nitrous oxide and 40% oxygen administered with a closed circle absorber Heidbrink anæsthetic machine. This percentage was obtained by running the nitrous oxide and oxygen at at least one litre per minute, along with periodic emptying and refilling of the rebreathing bag with fresh nitrous oxide and oxygen to replace the inert nitrogen: 30% of the flaxedil cases received minimal cyclopropane as well, usually near the end of the surgical procedure, and two cases received some ether. Five cases also received some d-tubo-curarine as well. In the curare series 25 patients received some cyclopropane and 3 cases some ether.

In the first few cases flaxedil was given after the induction of anæsthesia and as necessary during the operation to produce good operating conditions for the surgeon. Later, when its potency was better understood it was administered mixed with the $2\frac{1}{2}\%$ pentothal, 60 to 80 mgm. of flaxedil (20 mgm. to each c.c. of solution) being added to 0.5 gm. of pentothal dissolved in 20 c.c. of normal saline. This addition was made by drawing the flaxedil into a 5 c.c. syringe and then inserting the No. 23 G. needle into the tip of the 20 c.c. pentothal syringe with the latter's plunger withdrawn to make an air pocket and injecting the flaxedil fairly rapidly to achieve thorough mixing. No precipitate followed this mixing. Depending on the vigour of the patient and the contemplated operation any amount from no flaxedil up to 80 mgm. was injected into the second 20 c.c. syringe containing $2\frac{1}{2}\%$ pentothal. When intubation was to be performed, the patient was usually allowed to breathe 100% oxygen for two or three minutes following which an estimated dose of flaxedil was administered intravenously. The patient was then observed until he showed signs of discomfort or depressed

respiration, which usually occurred in about $1\frac{1}{2}$ to 2 minutes, at which time pentothal was given through the same needle in sufficient amounts and visual oral intubation performed. Intubation done in this manner insures peak action of the flaxedil and good oxygenation at the time of and following the intubation. Cyanosis does not occur. The depth of anæsthesia and relaxation needed for atraumatic easy oral intubation usually meant that apnoea was present during and for a few minutes following intubation. This was easily corrected by intermittent manual compression of the rebreathing bag before and after intubation. In

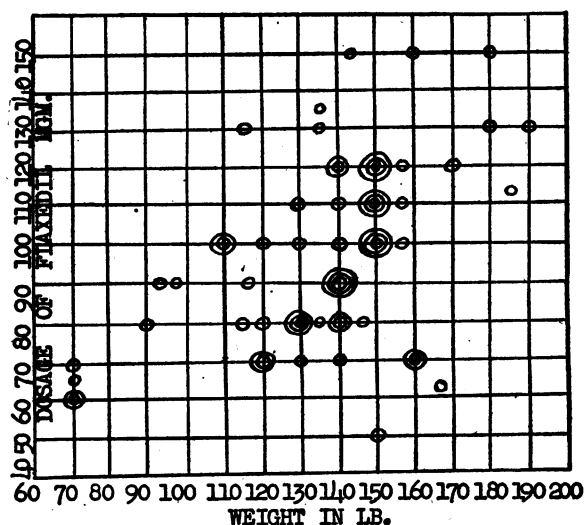


Fig. 1.—Illustrating the wide range of dosage needed in relation to weight to achieve comparable relaxation, i.e., sufficient relaxation for the first 45 minutes of a laparotomy or for easy oral intubation with light pentothal anæsthesia.

(Each circle represents one case.)

the curare series similar methods of mixing and administration of the drugs were used.

Dosage.—The average amount of flaxedil used in this series was 96.6 mgm. The largest amount was 220 mgm. for a gastrectomy and colectomy (carcinoma) in a 65-year old man in fair condition, weighing 190 lb. The operation lasted three hours and the patient did very well postoperatively. The smallest amount used was 40 mgm. for an appendectomy in a young man of 32, weighing 175 lb. and of a sedentary type. Anyone familiar with curare can gauge the necessary dose of flaxedil quite readily. It was soon apparent that as with curare, the amount of flaxedil needed was largely independent of the weight of the patient but very closely related to his or her vigour, age and muscular development. Thus young farmers

take the largest doses whereas obese elderly women of a sedentary occupation take the least. Fig. 1 illustrates the wide range of dosage used in relation to weight.

The dosage of each drug required to produce relaxation for the first 45 minutes of all the laparotomies in both series was averaged and compared and it was found that 15 mgm. of d-tubocurarine chloride was equivalent to 84 mgm. of flaxedil in relaxing power, or stated another way, 100 units of curare equals 84 mgm. of flaxedil, or again, 5 c.c. of curare equals approximately 4 c.c. of flaxedil (20 mgm. to each c.c. of flaxedil).

Preoperative state and complications.—Tables I to IV illustrate the types of operations, age, sex and estimated operative risks of the patients in both series. Table V illustrates the preoperative complications. It will be seen that all types of patients were included in the flaxedil and curare series and that many cases were poor risks.

Operative course.—Table VI shows the duration of the operations. It was noticeable that patients receiving flaxedil looked very well throughout their operations, being a normal slightly pink colour in most cases whereas those receiving curare not infrequently looked pale and occasionally slightly gray in colour.

TABLE I.

OPERATIONS PERFORMED WITH THE AID OF FLAXEDIL AND CURARE

	Flaxedil	Curare
Lobectomy.....	5	5
Thoracoplasty.....	1	0
Decortication lung.....	1	0
Craniotomy.....	3	3
Total gastrectomy.....	1	1
Partial gastrectomy.....	4	5
Cholecystectomy.....	9	9
Common bile duct.....	4	4
Other upper abdominal operations....	8	4
Pelvic operations.....	11	14
Appendectomy.....	7	7
Herniorrhaphy.....	5	6
Renal.....	2	2
Prostatectomy.....	1	0
Supra-pubic cystotomy.....	1	1
Lumbar sympathectomy.....	2	2
Head and neck.....	6	12
Thyroid (toxic).....	1	1
Radical Halstead.....	2	2
Perineal.....	6	7
Intervertebral discs.....	5	6
Extremities.....	8	4
Hæmorrhoids.....	6	5
Dilate œsophagus.....	1	0
Total.....	100	100

TABLE II.
AGE DISTRIBUTION—YEARS

	Flaxedil	Curare
Youngest.....	10.0	8
Oldest.....	86.0	80
Cases 70 and over.....	8.0	2
Cases 50 to 70.....	23.0	28
Average age.....	43.5	43

TABLE III.
SEX DISTRIBUTION

	Flaxedil	Curare
Male.....	51	42
Female.....	49	58
Total.....	100	100

TABLE IV.
ESTIMATED OPERATIVE RISK

	Flaxedil	Curare
Good.....	70	73
Fair.....	18	19
Poor.....	11	8
Serious.....	1	0
Total.....	100	100

TABLE V.
PREOPERATIVE COMPLICATIONS

	Flaxedil	Curare
Respiratory		
Simple cough or cold.....	22	19
Emphysema and/or severe cough.....	7	6
Bronchiectasis.....	6	7
Total.....	35	32
Cardiovascular		
Moderate hypertension.....	3	1
Moderate arteriosclerosis and/or severe hypertension.....	10	7
Auricular fibrillation and/or coronary occlusion or heart block.....	15	10
Total.....	28	18
Metabolic		
Jaundice.....	1	1
Diabetes.....	0	1
Toxic thyroid.....	1	1
Total.....	2	3
Neurological hemiplegia.....	1	0

TABLE VI.
DURATION OF OPERATIONS—MINUTES

	Flaxedil	Curare
Longest.....	250	180
Shortest.....	5	15
Average.....	63	80

Cardiovascular system.—It was noteworthy that the blood pressure was unusually well sustained when using flaxedil even when the patient's position had to be changed from the supine into the prone or lateral positions after the induction of anaesthesia. Only two cases had a systolic blood pressure under 100 mm. of Hg. at any time during or after their operations and then only for about 15 minutes each. In case No. 66, an 11-year old Indian girl, who was to have a lobectomy performed, the systolic blood pressure dropped from 120 to 75 mm. of Hg. following half a gram of pentothal and 80 mgm. of flaxedil for intubation. This was probably an overdose as controlled respiration was needed for the duration of the hypotension. The blood pressure had risen to 120 mm. of Hg. within about 15 minutes without any treatment and the operative course was uneventful except for a tachycardia of 150 to 160 per minute until near the end of the operation. The immediate preoperative pulse rate in this child was 160 per minute. Case No. 97, a woman of 61, was having an intervertebral disc exploration, after removal of a spinal bone graft, and bleeding from extra-dural veins was quite excessive. The systolic blood pressure was around 85 to 90 mm. of Hg. for ten minutes in this case. Eighteen cases in the curare series had a blood pressure under 100 mm. of Hg. at some time during the operation.

TABLE VII.
AVERAGE PULSE RATES

	Flaxedil	Curare
Immediate preoperative.....	101	96.0
Operative.....	102	88.8
Irregular pulse.....	4	2.0

The pulse rate (Table VII) was faster in most cases than is usual when curare is being used. This was never alarming and only excessive in two cases, No. 66, the Indian girl quoted above, and in case No. 72, a 48-year old man, a candidate for decortication of a chronic empyema, who had a blood pressure of 210/135, considerable expectoration and marked clubbing of the fingers. His pulse gradually rose to 145 per minute after being placed in the prone position. The blood pressure was well sustained despite extensive decortication of the lung. The pulse was 100 per minute four hours postoperatively. Despite these two cases many patients had an immediate preoperative pulse

rate of 110 to 130 per minute due to apprehension which settled to normal rates shortly after the induction of anaesthesia. This tachycardia has been avoided latterly by giving curare and flaxedil in about equal amounts to those patients in whom a tachycardia might be expected to occur, i.e., children, hypertensives, and the very ill or toxic patient. In this way a summation of the relaxant action of the two drugs is obtained without their bad effects.

The amount of bleeding was noted in most cases and a summary is contained in Table X comparing the flaxedil and curare cases. In no case was the bleeding serious and the arbitrary classification used was based on how much bleeding the anaesthetist and surgeon expected in any particular case. It will be seen that bleeding was apparently not affected by flaxedil. Blood transfusions were given as needed and the distinct impression was gained that the patients receiving flaxedil needed less blood administration than those cases which received curare. This was apparently due to a lack of a depressing action on the cardiovascular system of flaxedil.

Respiratory system.—Flaxedil, like curare, completely eliminated coughing and laryngospasm during anaesthesia. The respiratory rate varied from 12 to 60 per minute, being more rapid in light anaesthesia, and usually between 15 to 30 per minute. Table IX compares the

TABLE VIII.
ESTIMATED BLEEDING AT OPERATION

	Flaxedil	Curare
Sub-normal.....	35%	24%
Normal.....	47%	51%
Above normal.....	18%	25%

TABLE IX.
RESPIRATIONS DURING OPERATION

	Flaxedil	Curare
Normal throughout.....	42%	20%
Assisted or augmented respiration...	43%	67%
Artificial or controlled respiration...	15%	13%
Hiccoughs.....	5%	1%

effect of flaxedil and curare on the respiratory excursion. Assisted or augmented respiration was used in all cases where the slightest doubt of the adequacy of the tidal volume existed and in some cases the depression was probably due

to the pentothal, the preoperative sedation, or the position on the operating room table. It was often required only occasionally or intermittently. These cases are included in the table as requiring assisted respiration. Controlled or artificial respiration was seldom needed for more than five or ten minutes and was often needed following the deep anaesthesia used for intubation, 9 of the 15 patients receiving flaxedil, and needing controlled respiration, having been intubated.

It was noted when using flaxedil that when temporary apnoea occurred, due to excessive stimulation, as when pulling on the gall bladder or palpating the common bile duct, that the lungs were very easily inflated, which was not always the case when using curare in a similar light stage of anaesthesia. This inflation of the lungs during excessive stimulation is very easy when the patient is intubated. It is not so easy, but quite adequate when the patient is not intubated, due to a partial adduction of the vocal cords. Case No. 68 illustrates this. This was an extremely difficult cholecystectomy which necessitated constant and severe tugging on the gall bladder for about 20 minutes. Although the patient was not intubated a good respiratory exchange was maintained by intermittent manual compression on the rebreathing bag, although adductor spasm of the cords was present a good part of the time. It was of interest that immediately following the clamping of the cystic artery breathing became free and adequate and no more pentothal or flaxedil was required for the completion of the operation which lasted about one hour altogether. The blood pressure was unaffected and the pulse was between 100 and 110 per minute. The surgeon was quite impressed by the amount of trauma inflicted on the patient without a complaint from the anaesthetist. The patient was awake in the operating room immediately postoperatively.

Hiccoughs (Table IX) occurred in five cases receiving flaxedil. All these occurred during light anaesthesia and two of them at the precise moment that the mesentery of the appendix was clamped, presumably due to the stimulation of the sympathetic nerve supply in the mesentery. The other three cases occurred during a gastrectomy, while working on the duodenum, during a cholecystectomy when suturing the gall bladder bed, and the last

one while closing a perforated peptic ulcer. The hiccoughs in the last case were apparently precipitated on two occasions by starting assisted respirations. In four of the cases the hiccoughs ceased after deepening the anaesthesia while one case received intravenous procaine for the purpose. Baird¹⁰ reported a 3% incidence of hiccoughs during pentothal curare anaesthesia.

Perspiration was noted in three cases receiving flaxedil, this was not excessive and occurred during hot weather. The bowel was not affected one way or another, being neither dilated nor contracted and peristalsis was not especially in evidence. Priapism occurred in a boy of ten having an appendectomy performed with the aid of flaxedil. This persisted throughout the operation. The appendix was not acutely inflamed.

Postoperative course.—This was most satisfactory in both the curare and flaxedil series although the patients who had received flaxedil had a better colour in the immediate postoperative period. Over 50% of both series were awake by the time they reached the ward and 94% within half an hour of returning to the ward.

Practically all patients were seen at least once postoperatively and usually oftener. Nearly all the patients were up and walking, usually once around the bed, the same evening and at least t.i.d. thereafter. Postoperative complications are summarized in Table X. Atelectasis occurred following lobectomy in

TABLE X.
POSTOPERATIVE COMPLICATIONS

	<i>Flaxedil</i>	<i>Curare</i>
Respiratory		
Mild.....	6	5
Atelectasis.....	3	3
Total.....	9	8
Cardiovascular		
Mild circulatory depression.....	3	2
Severe circulatory depression....	0	0
Deep venous thrombosis.....	0	1
Total.....	3	3
Urinary		
Catheterized times one.....	3	2
Catheterized times two.....	1	1
Total.....	4	3
Vomit under 24 hours.....	17	19
Vomit over 24 hours.....	3	4
Total.....	20	23
Deaths.....	1	1

two cases in the curare series and in one lobectomy in the flaxedil series—the other cases of atelectasis followed upper abdominal operations. Any increase in the preoperative respiratory morbidity, apart from atelectasis, was classified as a mild respiratory complication.

The circulatory depressions (Table X) were mild and responded readily to simple electrolyte intravenous therapy, only one case (curare series) required blood postoperatively. Vomiting was about equally common in both series, and as expected, was much more common in women, 17 women vomiting and only 3 men in the flaxedil series. Eighteen women and 5 men vomited in the curare series. Mostly, the vomiting was mild in character and not violent nor unduly distressing. It was thought to be due to morphine or demerol in several cases, and in some cases appeared to be due to the unwise administration of fruit juice or jelly on the same day as the operation.

Urinary retention was not a serious factor in any case and always subsided when the patient could get to a toilet or a commode.

Bilateral deep thrombosis of the leg veins occurred in one case in the curare series. This responded to dicoumarol therapy and ambulation was continued. This patient had nearly died from a pulmonary embolus several years ago following an appendectomy.

There was one death in each series. The patient in the flaxedil series was a man of over 50 years of age who was brought to the operating room in a semi-moribund state and suffering from a recent hemiplegia. He had bilateral burrholes made in the parietal regions of his skull and some yellowish subdural fluid evacuated on each side. He died 4 days postoperatively. Post-mortem revealed a large left cerebral hæmorrhage and moderate conus medullaris.

The death in the curare series followed a drainage of the common bile duct in a 60-year old woman with severe progressive jaundice (icterus index 176) and subacute hepatitis. No disease of the bile ducts was present and she was overtreated with sodium chloride intravenously postoperatively, developed marked generalized oedema on the third day, and died in coma on the sixth day postoperatively. Post mortem revealed acute yellow atrophy of the liver. It is felt that neither death was related to the drugs used.

Six cases in the flaxedil series were given prostigmine 0.5 to 1.5 mgm. (1/2,000 solution) along with atropine 1/150 to 1/200 gr. at the end of the operation. These were all short operations where good relaxation was needed for the procedure, but the respiration was not considered adequate at the termination of the operation. The prostigmin was effective within 5 minutes in each case.

DISCUSSION

It would seem from the experiences with the cases outlined above that flaxedil is a useful addition to the anæsthetist's armamentarium. As with curare, patients can be subjected to all forms of surgery while receiving only small doses of relatively non-toxic anæsthetic agents. It is superior to curare in that bronchospasm and hypotension do not occur and that respiration is less depressed with comparable relaxant doses. A disadvantage is the occasional occurrence of a tachycardia which, however, seems harmless and is self-limited.

Contraindications to the use of flaxedil are the same as curare, *i.e.*, myasthenia gravis and possibly asthma, although it would appear to be a safer drug than curare in asthmatics. In addition it would seem advisable not to use it or to use only small doses where a tachycardia exists or seems likely to occur under anæsthesia, *e.g.*, in hypertensives or severe toxic states. This tachycardia would appear to limit the use of the drug in very young children.

Smaller doses of flaxedil would be adequate where cyclopropane or ether was the main anæsthetic.

It should be noted that adequate operating conditions obtained throughout all these anæsthetics.

SUMMARY

1. The properties of a relatively new muscle relaxant drug (flaxedil) have been reviewed.
2. Clinical results of its administration to 100 patients undergoing surgery have been described and compared with 100 similar patients who received curare.
3. Contraindications are stated.

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RÉSUMÉ

L'auteur résume son expérience avec l'emploi du flaxédyl chez cent opérés par comparaison à cent autres où le curare fut employé. Ce nouvel agent curarisant de synthèse est une addition de valeur aux médicaments employés couramment par l'anesthésiste. Comme avec le curare le patient peut subir n'importe laquelle intervention chirurgicale tout en ne recevant que de très petites doses d'agents anesthésiques. Il est supérieur au curare parce qu'il ne produit pas ni de spasme bronchique ni d'hypotension. De plus la respiration est déprimée à un moindre degré. Cependant l'auteur a souvent remarqué qu'une tachycardie d'ailleurs bénigne se produisait. Les contre-indications sont les mêmes qu'avec le curare. Il n'est pas nécessaire d'employer d'aussi grosse dose qu'avec le curare lorsque le cyclo est l'agent anesthésique. YVES PRÉVOST

CONVULSIONS AND HEMIPLEGIA IN PERTUSSIS PROPHYLAXIS

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MILD to moderately severe local and febrile reactions to pertussis vaccine are commonly encountered, and have not caused great concern. Recent studies in the United States have, however, indicated that grave reactions may occur on rare occasions following the use of pertussis vaccine and other biological products. These include convulsive seizures with or without permanent cerebral damage. A number of these have ended fatally. Such reactions have not been reported in Canada to date, despite the widespread use of pertussis vaccine over the past decade.

As early as 1933 Madsen¹ reported that two infants in Denmark in the neonatal period had died shortly after the administration of pertussis vaccine. In 1948 Byers and Moll² reported in detail on encephalopathy following the use of this vaccine. During the period between 1939 and 1947 there had been fifteen instances in which admissions had been made to the Children's Hospital of Boston for this complication; two of these cases died. In the same period there were 8 admissions for cerebral damage following smallpox vaccination, and 26 cases in which encephalopathies occurred following pertussis infection. They also reviewed the literature on these complications in pertussis prophylaxis.

In 1949 Toomey³ reported on information received after solicitation from a large number of physicians who were concerned with pertussis immunization. The replies indicated 38 instances in which reactions occurred that were sufficiently severe to produce convulsions. Two of these cases are known to have died.

Following are descriptions of two cases in which severe untoward reactions occurred after administration of the triple antigen preparation* most commonly used in this country at the present time.

CASE 1

C.H., a white female infant of seven months received the first dose of multiple antigen in my office on May 28, 1948. Five hours later the mother noticed a general reaction consisting of fever with malaise and irritability. Nine hours after inoculation the mother reported the occurrence of a convulsion, and the baby was seen in the early stage of seizure. The clonic movements were predominantly right-sided, involving the right arm, right leg, and right side of the face; the head was kept turned to the right. In spite of the evident deep coma, shrill shrieking noises were emitted during the most violent phase of the seizure, which lasted well over two hours. The highest rectal temperature recorded during the convulsive seizure and afterwards was 102°. Phenobarbital sodium and rectal chloral hydrate were used to control the spasms.

Twitchings of the right side of the body recurred for the next two days in milder form. On admission to the London War Memorial Children's Hospital, on May 31, Dr. H. S. Little was consulted. There was little active use of the right arm and leg and there was paresis of the right sixth and seventh cranial nerves. Mild twitchings of the right side of the body continued, and spasticity was noted in the right arm and leg. The eyegrounds appeared normal. It was felt at this time that some permanent cerebral damage had occurred involving principally the left cerebral hemisphere. On June 2 the patient was transferred to the Toronto Hospital for Sick Children for further investigation. On discharge from that hospital two days later there was slight noticeable improvement in voluntary movement of the affected arm and leg; the twitchings had ceased.

Spinal fluid was under normal pressure; 2 cells per c.mm.; 25 mgm. total protein, 60 mgm. sugar, 745 mgm. chlorides %. Colloidal gold reaction was negative. Hb. 12.6 gm. %, white blood cells 8,200. Blood Wassermann was negative. Serum Ca. 11.1 and P. 4.8 mgm. %. Fasting blood sugar 110 mgm. %.

Further progress.—On June 30, neurological examination was made by Dr. W. S. Keith in Toronto. He reported that there was fairly good return of function of the sixth and seventh cranial nerves, but due to persistence of hemiparesis of right arm and leg, he felt that there had been considerable and fairly persistent damage to the left parietal and frontal lobes.

On September 12, the patient was again admitted to the War Memorial Children's Hospital in a convulsive seizure accompanying an attack of acute otitis media. On this occasion the rectal temperature rose to 104° F. The convulsion was rapidly controlled and recovery was prompt when the acute infection subsided. There was no evidence of further residual encephalopathy following this episode.

Improvement of function of the right leg has been greater than that of the right arm. She was able to walk unaided at fifteen months of age. At first the gait was of the typical hemiplegic type with the right

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